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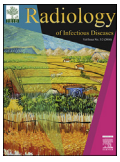

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Editorial

Neuroinfection & neuroimmunology: New opportunities, new challenges

Neuroinfection & neuroimmunology is a growing subspecialty of the nervous system. Despite remarkable diagnostic and therapeutic advancements during the past 30 years through the prevention of infectious diseases by vaccine and the development of safe, effective antimicrobial agents, neurologic infections remain to be major causes of permanent neurologic disability worldwide [1]. In this issue of *Radiology of Infectious Diseases*, the articles succinctly cover a range of radiologic topics of infectious or immunological diseases of the central nervous system (CNS), focusing on some areas of controversy and current hot topics. The goal is to summarize the ongoing challenges in CNS infectious or immunological diseases and suggest potential areas for further exploration.

Viruses may invade any part of the CNS and cause both acute and chronic neurologic diseases. Viruses constitute the most common infectious cause of encephalitis, aseptic meningitis, and myelitis. Unique disorders appear episodically in human populations and cause life-threatening systemic or neurological diseases [2]. Over 100 viral pathogens can affect the CNS, with varied clinical manifestations. Historical examples of such disorders include von Economo encephalitis, acquired immune deficiency syndrome (human immunodeficiency virus infection) and severe acute respiratory syndrome. In addition to the more commonly reviewed syndromes of meningitis, encephalitis, and myelitis, less frequent but characteristic syndromes are important to be recognized. Recently, some novel avian influenza A(H1N1), A(H7N9), A(H5N1), A(H5N6) viruses or even recently reported Zika virus (ZIKV), for their fatal attack to CNS, have drawn great attentions all over the world [3–5]. Specifically, the pandemic of swine-origin H1N1 influenza that began in early 2009 had provided evidence that radiology could assist in the early diagnosis of severe cases, providing new opportunities for the development of advanced infectious disease imaging [3]. Dr. Shi also suggested findings of high-resolution lung CT correlated with $CD4^+$ and $CD8^+$ lymphocyte counts and the C-reactive protein level in the peripheral blood in the initial stage of adult patients with H1N1 influenza. The sophisticated current imaging techniques enable us to study influenza at the cellular level, in animal models, and in human clinical trials to elucidate the pathogenesis of severe illness and improve clinical outcomes. Middle Eastern respiratory syndrome (MERS) is a new illness caused by the Middle East respiratory syndrome coronavirus (MERS-CoV). MERS-CoV infection should be suspected in patients presenting with risk factors of MERS-CoV infection, suspicious clinical, laboratory results and chest CT scans showing ground-glass opacities with a preference for the peripheral lower lobe [6]. Ebola infections in West Africa have been a major news story in the past two years. As of October, 2015, nearly 18,000 cases have been reported, with about 6500 deaths, with the infection spreading rapidly because the virus is present in all body fluids, including sweat and mucous membrane secretions. Radiology workup does not provide specific diagnosis of Ebola virus infection, however, it is indispensable to prognostic assessment in the emergency department and treatment isolation care unit [7]. The classic clinical picture of ZIKV infection is manifested by fever, headache, arthralgia, myalgia, and maculopapular rash. A major concern associated with this infection is the apparently increased incidence of microcephaly in fetuses born to mothers infected with ZIKV. Ultrasonography can reveal microcephaly with calcifications in the fetal brain and placenta [5]. Quantitative assessment of lung abnormalities based on chest radiographic and CT scores should allow clinicians to accurately monitor disease progression and provide information regarding patient prognosis. The radiologists should play a critical role in the monitoring of patients with viral infection [6,7].

Despite notable improvements in disease prevention and treatment, infectious diseases of the CNS remain an important source of morbidity and mortality, particularly in less-developed countries and in immunocompromised individuals. Bacterial, fungal, and parasitic pathogens are derived from living organisms and affect the brain, spinal cord, or meninges. Infections due to these pathogens are associated with a variety of neuroimaging patterns that can be appreciated at MRI in most cases [8]. In this issue, Dr. Zhang et al. retrospectively analyzed the clinical and MRI features of cerebral

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paragonimiasis in 24 pediatric cases. Although the clinical manifestations of cerebral paragonimiasis were nonspecific, but MRI findings were characteristic, including irregular hemorrhage, ring-like enhancement and incommensurately larger range of edema. Therefore, MRI plays avital role in the diagnosis of cerebral paragonimiasis in children. Dr. Li et al. also retrospectively analyzed the imaging findings of 22 cases serologically and clinically confirmed as *Paragonimus westermani* infection during past five years. They suggested that the imaging findings of *P. westermani* were diverse and nonspecific due to their complex life cycle and several life stages during infestation of human; however, the common features included patchy low or mixed density lesions on brain CT and ring-enhancing lesion on brain MRI. The presences of worm cyst and migration track were considered to be the characteristic imaging features of paragonimiasis. CT is probably useful in a few patients to identify calcification and hemorrhage, typically occurred during the acute stage and in the early stages of further Paragonimus migration [9]. Routine MRI shows great advantages on the presence and degree of infections, the host response to the infection. Advanced MRI techniques such as MR spectroscopy (MRS) have provided a surrogate marker of tissue chemical information, thereby could differentiate parasitic infections from other infections and also possibly monitor therapeutic response. Early detection and diagnosis of bacterial infections involving the CNS are paramount. Utilizing the clinical information in conjunction with the imaging findings is necessary to optimize treatment and ultimately improve patient care and thus reduce mortality and morbidity. Early neurosurgical intervention is advocated to prevent the ongoing risk of serious complications [10]. Therefore, pre-operative imaging workup plays a critical role in procedure planning and prognosis assessment in bacterial infection of the CNS.

Autoimmune and immune-mediated mechanisms are increasingly appreciated in many neurologic diseases. Neuromyelitis optica (NMO) is an autoimmune, demyelinating disorder of the CNS with typical clinical manifestations of optic neuritis and acute transversemyelitis. The discovery of autoantibodies against aquaporin-4 (AQP4-IgGs) changed our understanding of NMO immunopathogenesis and revolutionized the diagnostic algorithm [11]. As we have known, Wernicke encephalopathy (WE) and NMO are totally different disease entities. However, the similar lesion locations may potentially imply that there may be some correlations between them, and astrocytes may be the common target involved. The use of advanced MRI techniques may enhance our understanding of the pathogenic processes in CNS inflammatory diseases and help us identify the distinct radiologic features corresponding to specific phenotypic manifestations. Correlation between the underlying pathophysiologic mechanism of immunological diseases and imaging findings has been fully elucidated. MRI remains the imaging modality of choice in demonstratingthe early signs of infection/inflammation [12]. Furthermore, DWI and MRS also show great promise in detecting early changes than conventional MRI and provide more specific information regarding the etiology of signal abnormalities seen on conventional MRI. Chemical exchange saturation transfer (CEST) is a novel MRI technique for specifically detecting slow-to-intermediate exchange rate of protons associated with proteins and neurochemicals with water [13]. In this issue, Dr. Wu comprehensively reviewed the interactions between activated microglia and astrocytes in the early stages of neuroinflammation and summarized the insights provided by MRS and CEST. Experimental and clinical studies were also reviewed to emphasize the contributions of MRS and CEST in investigating the pathophysiology and evolution in the early stages of neuroinflammation.

The articles of this issue have provided thorough and illustrative discussions of these emerging and challenging topics in CNS infectious & immunological diseases, and we are indebted to the authors for their hard work and expertise. The upcoming decades are sure to provide us with an ever-evolving landscape of infection, inflammation, and immunology. As imaging specialists, we are encountering more opportunities and facing more challenges.

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